

REMARKS

Upon entry of the present amendment, claims 70, 119-121, 123-129, 131 and 132 are pending in the above-referenced patent application and are currently under examination. Claims 70, 119-121, 129 and 131 have been amended. Claims 118, 122 and 130 have been canceled. Claims 123 and 124 have been withdrawn. Reconsideration of the application is respectfully requested.

Claims 70, 120, and 121 have been amended to remove dependency on canceled claim 118.

Claim 119 has been amended to change “aryl” to phenyl.” Support for this amendment can be found throughout the specification, particularly at in the definition of “aryl” at paragraph [0055] and in paragraph [0067] providing that “phenyl” is a preferred embodiment.

Claim 129 has been amended to remove compounds encompassed by canceled claim 118.

Claim 131 has been amended to remove reference to radical m which is not in the claim.

Applicants believe no new matter has been added by the amendments to the claims.

The claims are rejected in various combinations under 35 U.S.C. §§ 102(a), 102(e), 103(a) and 112, 2d. In addition, claims 70, 120, 121 and 129 have been objected to. Each of these rejections and objections is addressed below in the order set forth by the Examiner.

I. OBJECTIONS

Claims 70, 120 and 121 have been objected to as being dependent on withdrawn claim 118. Applicants note that claim 118 has been canceled and claims 70, 120 and 121 amended to depend from only claim 119. Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the objection.

Claim 129 has been objected to as failing to use commas between the species, and failing to provide an “and” between the last two species. Applicants note that the species

without the comma have been removed from claim 129. Furthermore, claim 129 has been amended to recite an “and” between the last two pending species. Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the objection.

II. INDEFINITENESS REJECTION UNDER 35 U.S.C. § 112, 2d PARAGRAPH

Claim 131 has been rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Applicants respectfully traverse the rejection in view of the comments below.

The test for indefiniteness is “whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity” (MPEP § 2173.02). This analysis does not occur in a vacuum, but rather in view of the following factors: (1) the content of the particular application disclosure; (2) the teachings of the prior art; and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. In addition, “the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope” (MPEP § 2173.02).

The Examiner notes that there is no radical “m” in the formula, but that a radical “m” is defined. Applicants note that the definition of radical “m” in claim 131 has been removed. Thus, amended claim 131 is not indefinite under 35 U.S.C. § 112, 2d paragraph. Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the rejection.

III. FIRST ANTICIPATION REJECTION UNDER 35 U.S.C. § 102(a) BY MORISSEAU

Claims 129, 131 and 132 have been rejected under 35 USC § 102(a) as allegedly being anticipated in view of Morisseau. Applicants respectfully traverse the rejections in view of the comments below.

A claim is considered to be anticipated under 35 USC § 102(a) if “the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.” In order for

a claim to be anticipated by a reference, the reference must teach every element of the claim (MPEP § 2131, citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). As discussed in detail below, the presently claimed invention is not anticipated in view of any of the cited references as all the references fail to teach every element set forth in the claims of the instant invention.

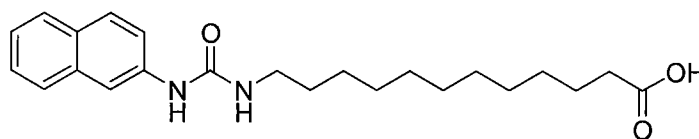
Applicants submit herewith an *In re Katz* declaration under 37 CFR 1.132, establishing that Morisseau describes the inventors' own work, as disclosed in the priority application, U.S. Application No. 60/460,559, filed April 3, 2003. The declaration is executed by Dr. Newman, a joint inventor of the present application. This declaration with the signature of Dr. Newman provides the missing signature of the declaration submitted July 9, 2007 executed by Drs. Morisseau and Hammock.

In view of the fully executed *Katz* declaration, Applicants submit that Morisseau is not prior art to the instant application under 35 U.S.C. §§ 102(a) or 102(e). Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the rejection.

IV. SECOND ANTICIPATION REJECTION UNDER 35 U.S.C. § 102(a) BY KROETZ

Claims 70, 119-122 and 125-128 have been rejected under 35 USC § 102(a) as allegedly being anticipated in view of Kroetz. Applicants respectfully traverse the rejections in view of the comments below.

The Examiner alleges that compound 283 of Kroetz falls within the scope of the pending claims:



Compound 283 of Kroetz has a naphthyl group in the R¹ position of formula (I) of claim 119. Applicants note that claim 119 has been amended to recite that R¹ is selected from "phenyl and heteroaryl." R¹ of amended claim 119 does not encompass naphthyl.

As the naphthyl group of Kroetz compound 283 is not encompassed by R¹ of amended claim 119, Kroetz compound 283 fails to disclose all the elements of amended claim 119, and dependent claims 70, 120-122 and 125-128. Thus, the amended claims are anticipated

under 35 U.S.C. § 102(a) by Kroetz. Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the rejection.

V. THIRD ANTICIPATION REJECTION UNDER 35 U.S.C. § 102(e) BY KROETZ (I)

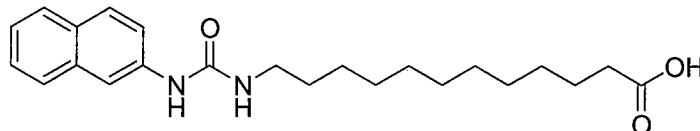
Claims 70, 119-122 and 125-128 have been rejected under 35 USC § 102(e) as allegedly being anticipated in view of Kroetz (I). Applicants respectfully traverse the rejections in view of the comments below.

A claim is considered to be anticipated under 35 USC § 102(e), when filed after November 29, 2000, if

the invention was described in - (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

In order for a claim to be anticipated by a single reference, the reference must teach every element of the claim (MPEP § 2131, citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). As discussed in detail below, the presently claimed invention is not anticipated in view of any of the cited references as each reference fails to teach every element set forth in the claims of the instant invention.

As noted above, the Examiner alleges that compound 283 of Kroetz (I) falls within the scope of the pending claims:



Compound 283 of Kroetz (I) has a naphthyl group in the R¹ position of formula (I) of claim 119. Applicants note that claim 119 has been amended to recite that R¹ is selected from “phenyl and heteroaryl.” R¹ of amended claim 119 does not encompass naphthyl.

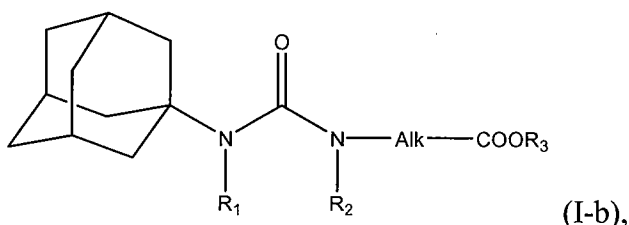
As the naphthyl group of Kroetz (I) compound 283 is not encompassed by R¹ of amended claim 119, Kroetz (I) compound 283 fails to disclose all the elements of amended claim 119, and dependent claims 70, 120-122 and 125-128. Thus, the amended claims are anticipated under 35 U.S.C. § 102(e) by Kroetz (I). Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the rejection.

VI. OBVIOUSNESS REJECTION UNDER 35 U.S.C. § 103(a) OVER RICHTER, BROCCINI & ABDULLA

Claims 129, 131 and 132 have been rejected under 35 USC § 103(a) as allegedly being obvious over the combination of Richter, Brocchini and Abdulla. Applicants respectfully traverse the rejection in view of the comments below.

A claim is considered obvious “if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains” (35 USC § 103(a)). The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1395-97 (2007) identified a number of rationales to support a conclusion of obviousness which are consistent with the proper “functional approach” to the determination of obviousness as laid down in *Graham*. The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR* noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. One of the rationales addressed by the court in *KSR* supports a finding of obviousness when the prior art reference (or combination of references) (1) teaches or suggests the claim elements; (2) provides some suggestion or motivation to combine the references; and (3) provides a reasonable expectation of success (MPEP § 2143). As discussed in detail below, none of the cited references satisfies all three requirements under MPEP § 2143.

Richter discloses



where Alk is 1 to 10 carbons. R_3 is selected from the group of hydrogen, a straight or branch chained saturated alkyl of from 1 to 12 carbons, di-(lower alkyl)-amino-lower alkyl, benzyl, 4-(N-methyl)-piperidyl and an alkoxy group of the formula: $R'-(O-R'')_n-O-R'''$, where R' , R'' , and R''' are each a member selected from the group consisting of methyl and ethyl, and n is an integer from zero to three.

By comparison, the compounds of amended claims 129, 131 and 132 have an alkylene linker of 11 or 12 carbons. Richter *et al.* does not teach compounds having an alkylene linker of 11 or 12 carbons.

As noted above, the test for non-obviousness was recently addressed by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) where the court rejected a rigid application of the teaching, suggestion, or motivation (TSM) test. In regards to chemical compounds, the Court of Appeals for the Federal Circuit recently held in *Takeda Chemical Industries Ltd. v. Alphapharm Pty. Ltd.*, 83 USPQ.2d 1169 (Fed. Cir. 2007) that:

While the KSR Court rejected a rigid application of the teaching, suggestion, or motivation (“TSM”) test in an obviousness inquiry, the Court acknowledged the importance of identifying “a reason that would have prompted a person skilled in the relevant field to combine the elements in the way the claimed new invention does” in an obviousness determination. *KSR*, 127 S. Ct. at 1731. Moreover, the Court indicated that there is “no necessary inconsistency between the idea underlying the TSM test and the Graham analysis”. *Id.* As long as the test is not applied as a “rigid and mandatory” formula, that test can provide “helpful insight” to an obviousness inquiry. *Id.* Thus, *in many cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish a prima facie case of obviousness.*¹ (emphasis added)

¹ In *Takeda*, the patented compound had a 5-ethyl substituent and the prior art compound had a 6-methyl substituent. Alphapharm, the generic drug manufacture sued by Takeda, the patent holder, for infringement, alleged that one of

The Examiner is reading more into Richter *et al.* than Richter *et al.* actually teaches. Richter *et al.* teaches anti-viral compounds having an alkyl chain up to 10 carbons. Richter *et al.* limits the alkyl chain to 10 carbons because Richter reasonably expected that a carbon chain up to 10 carbons would provide anti-viral activity, but that a carbon chain with more than 10 carbons would not. The examiner has not identified a reason for a chemist to modify compounds disclosed in Richter *et al.* by extending the carbon chain length from 10 to 11 or 12.

Furthermore, it is a long held axiom of patent law that questions of chemical obviousness cannot be decided on the basis of structure alone. See, *In re Papesch*, 3 15 F.2d 38 1,137 USPQ 43 (CCPA 1963). The inquiry into the patentability of the presently claimed compounds must also extend to the properties that they exhibit. Homology is nothing more than a fact that must be considered with all other relevant facts. *In re Mills*, 28 1 F.2d 2 18,224, 126 USPQ 5 13 (CCPA 1959). Specifically, the Court of Customs and Patent Appeals expressed that “[h]omology should not be automatically equated with *prima facie* obviousness.” See, *In re Lancer*, 465 F.2d 896, 899; 175 U.S.P.Q. 169, 171 (CCPA 1972). When making an obviousness determination, the prior art and the claimed subject matter must be viewed “as a whole.” *Id.*

In this case, we believe that when viewed as a whole, Richter *et al.* does not render the claimed invention obvious. As described above, Richter *et al.* specifically defines Alk as having 1 to 10 carbons, while allowing R₃ to have 1 to 12 carbons. If there had been any suggestion in Richter *et al.* that compounds having 11 or 12 carbons as Alk would also possess anti-viral activity, Richter *et al.* could have defined Alk as having from 1 to 12 carbons as the definition for R₃. By not doing so, Richter *et al.* suggests that Alk being 10 and R₃ being 12 are the limit for anti-viral activity for compounds of formula (I-b). A person skilled in the art would be led to believe that compounds with Alk being more than 10 carbons would not have anti-viral activity.

skill in the art would have been motivated to select the prior art compound as the lead compound. Alphapharm further alleged that it would have been obvious to one of skill in the art to make two obvious chemical changes: first, homologation and second, ring walking. The district court and the Federal Circuit disagreed, holding that there was no motivation to make the chemical changes, thus upholding that the 5-ethyl compound is not obvious over the 6-methyl compound.

Therefore, viewed as a whole, the invention disclosed in Richter et al. does not make the presently claimed invention obvious under 35 U.S.C. § 103(a). Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the rejection.

VII. FIRST OBVIOUSNESS-TYPE DOUBLE PATENTING OVER THE '685 APPLICATION

Claims 70, 119-122, 125-129, 131 and 132 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 and 28-60 of the '685 application (claims of March 3, 2006).

Pursuant to MPEP § 804 I(B)1:

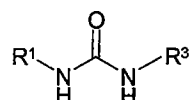
If a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer.

Following withdrawal of the rejections above and below in the instant application, the provisional obviousness-type double patenting rejection based on the '685 Application will be the only remaining rejection. In addition, the '685 Application, which is the later-filed application, has not yet been examined on its merits. Accordingly, under MPEP § 804 I(B)1, this rejection can be withdrawn following withdrawal of all other rejections.

VIII. SECOND OBVIOUSNESS-TYPE DOUBLE PATENTING OVER THE '641 APPLICATION

Claims 70, 119-122, 125-129, 131 and 132 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 46 of the '641 application (claims of October 29, 2007).

The now pending claims of the '641 Application are directed to methods of reducing blood pressure in a patient, by administering a therapeutically effective amount of an epoxide hydrolase inhibitor. More specifically, the epoxide hydrolase inhibitor has the following formula:



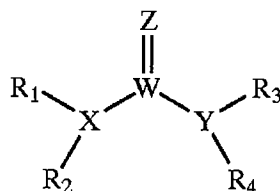
where R¹ and R³ are each independently selected from the group consisting of C₁-C₂₀ substituted or unsubstituted alkyl, cycloalkyl, aryl, acyl and heteroacyclic. (This description is not intended to replace or modify the claims of '641 Application)

The instant claims are directed to compounds having narrowly defined structures with an additional tertiary pharmacophore, which provide the unexpected improvement in potency and physical properties. Therefore, the instant claims are patentably distinct over the pending claims of the '641 Application. Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the rejection.

IX. THIRD OBVIOUSNESS-TYPE DOUBLE PATENTING OVER THE '506 PATENT

Claims 70, 119-122, and 125-128 have been rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of the '506 patent.

Claims 1-11 of the '506 Patent claims a method of treating hypertension by administering a therapeutically effective amount of an epoxide hydrolase inhibitor. More specifically, the epoxide hydrolase inhibitor has the following formula:



wherein W can be carbon, phosphorous or sulfur, more specifically carbon, X and Y can be nitrogen, oxygen or sulfur and more specifically nitrogen, R₁ and R₃ can be C₁-C₂₀ substituted or unsubstituted alkyl, cycloalkyl, aryl, acyl, or heterocyclic. (This description is not intended to replace or construe the claims of '506 Patent) The specific compound recited in the claimed method is dicyclohexylurea.

The instant claims are directed to compounds having narrowly defined structures with an additional tertiary pharmacophore, which provide the unexpected improvement in potency and physical properties as described in the specification at paragraph [0060]. Data supporting the unexpected increase in potency are provided in Table 4, where all compounds listed have IC₅₀ values less than 0.3 mM for both mouse and human sEH. Therefore, the instant claims are patentably distinct over claims of the '506 Patent. Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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Attachments
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